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ORIGINAL ARTICLE

Off-pump surgery for the poor ventricle?

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Abstract Severely decreased ejection-fraction is an established risk-factor for worse outcome after cardiac surgery. We compare outcomes of off-pump coronary artery bypass grafting (OPCAB) and on-pump CABG (ONCABG) in patients with severely compromised EF. From 2004 to 2009, 478 patients with a decreased EF ≤35% underwent myocardial-revascularization. Patients received either OPCAB ($n = 256$) or ONCABG ($n = 222$). Propensity score (PS), including 50 preoperative risk-factors, was used to balance characteristics between groups. PS adjusted logistic regression analysis was performed to assess mortality and major adverse cardiac and cerebrovascular events (MACCE). A composite endpoint for major non-cardiac complications such as respiratory failure, renal failure, rethoracotomy was applied. Complete revascularization (CR) was assumed when the number of distal anastomoses was larger than that of diseased vessels. There was no difference for mortality (2.3 vs. 4.1%; PS-adjusted odds ratio (PS-OR) = 1.05; $p = 0.93$) and MACCE (13.7 vs. 17.6%; PS-OR = 1.22; $p = 0.50$) including myocardial-infarction (1.4 vs. 4.9%; PS-OR = 0.39; $p = 0.26$), low cardiac output (2.3 vs. 4.7%; PS-OR = 0.75; $p = 0.72$) and stroke (2.3 vs. 2.7%; PS-OR = 0.69; $p = 0.66$). OPCAB patients presented with a trend to less frequent occurrence of the non-cardiac composite (12.1 vs. 22.1%; PS-OR = 0.54; $p = 0.059$) including renal dysfunction (PAOR = 0.77; 95% CI 0.31–1.9; $p = 0.57$), bleeding (PAOR = 0.42; 95% CI 0.14–1.20; $p = 0.10$) and respiratory failure (PAOR = 0.39; 95% CI 0.05–3.29; $p = 0.39$). The rate of complete revascularization was similar (92.2 vs. 92.8%; PS-OR = 0.75; $p = 0.50$). OPCAB in patients with severely decreased EF is safe and feasible. It may even benefit these patients in regard to non-cardiac complications and does not come at cost of less complete revascularization.

Keywords Ejection fraction · Off-pump surgery · Coronary artery bypass grafting · Heart failure

Introduction

Surgical revascularization for patients with severe left ventricular dysfunction remains a challenge. Various studies report an increased peri-operative mortality and morbidity for these patients [1, 2]. In the EuroScore risk stratification system (http:\\www.euroscore.org), decreased ventricular function is an independent risk factor for worse outcome after cardiac surgery.

Conventional CABG is performed with cardio-pulmonary bypass (CBP), which is associated with complications such as renal dysfunction, stroke, and other neurological complications [3] as well as an increased risk for a systemic inflammatory response syndrome (SIRS) [4]. The compromised outcomes for patients undergoing CABG with ventricular dysfunction may be in part linked to the use of CPB and the application of cardioplegic solutions to achieve cardiac arrest [4, 5].

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Off-pump coronary artery bypass surgery (OPCAB) has a comparable risk-adjusted mortality and morbidity as on-pump CABG [6–8]. Current reports suggest OPCAB to be superior for high-risk patients [9]. For patients with severe ventricular dysfunction, only few reports are available [10–13].

In this study, we evaluate safety and feasibility of OPCAB surgery in patients with a decreased ejection fraction (≤35%).

Materials and methods

From 2004 to 2009, 3,981 patients underwent surgical revascularization at our institution. Of these patients, 478 presented with severe ventricular dysfunction and an ejection fraction ≤35%. Of these, 53% ($n = 256$) received off-pump surgery (OPCAB) and 47% ($n = 222$) conventional CABG. All data were collected prospectively and the study was approved by an institutional review board (IRB), including a waiver of informed consent. Indication for surgery was: elective (66.8 vs. 64.4%; $p = 0.63$), urgent (32.4 vs. 27.7%; $p = 0.27$), and emergent (5.5 vs. 3.2%; $p = 0.26$) respectively. The EuroScore (http:\\www.EuroScore.org) was used for preoperative risk stratification. The ejection fraction was documented by preoperative transthoracic echocardiography and was confirmed with in a left ventriculogram, which was obtained during coronary angiography to define the target vessels. In addition, these data were correlated to intraoperative trans-esophageal echocardiography (TOE) in all patients as TOE is part of our OPCAB practice (Table 1).

Table 1 Preoperative characteristics and demographics

Parameter	OPCAB $n = 256$	CABG $n = 222$	p value
Age (years)	64 ± 10	63 ± 9	0.27
Male (%)	81	85	0.22
Female (%)	19	15	0.23
EuroScore	4.6 ± 1.0	4.9 ± 1.0	0.06
BMI (kg/m^2)	27 ± 4	27 ± 4	0.54
Elective (%)	66.8	64.4	0.63
Urgent (%)	32.4	27.7	0.27
Emergent (%)	5.5	3.2	0.26
Sinus rhythm (%)	91.6	98.6	0.002
Atrial fibrillation (%)	4.9	0.9	0.03
Pacemaker (%)	3.5	0.5	0.04
No. of diseased vessels	2.79 ± 0.45	2.95 ± 0.23	0.001
1-vessel disease (%)	1.5	2.3	0.74
2-vessel disease (%)	18.4	11.7	0.56
3-vessel disease (%)	80.1	86.0	0.09
Left main disease (%)	28.5	23.9	0.26
CCS 1 (%)	7.6	7.2	1.00
CCS 2 (%)	29.4	28.4	0.83
CCS 3 (%)	42.2	36.9	0.28
CCS 4 (%)	20.9	27.5	0.11
NYHA 1 (%)	51.5	49.5	0.70
NYHA 2 (%)	26.4	22.1	0.32
NYHA 3 (%)	19.5	17.1	0.55
NYHA 4 (%)	2.6	11.3	0.001
Redo surgery (%)	5.5	4.5	0.68

EF ejection fraction, *BMI* body mass index, *CCS* Canadian Cardiovascular Society Angina Classification, *NYHA* New York Heart Association

Surgical technique

CABG was performed with administration of standardized cardio-pulmonary bypass techniques and proximal anastomosis was done with cross-clamping of the aorta. OPCAB procedures were performed as previously described [14]. Briefly, heparin was given to achieve an active clotting time (ACT) in excess of 350 s. Pacemaker wires were placed epicardially, before a stabilizer (Octopus®4 Tissue Stabilizer, Medtronic, Minneapolis, USA) was applied for target vessel exposal. Shunt insertion was (ClearView® Intracoronary Shunt, Medtronic, Minneapolis, USA) was routinely performed to maintain distal perfusion during anastomosis and a mister blower (Guidant, Indianapolis, USA) with CO_2 and water was used to clear the surgical field. If no T-Graft was performed and whenever a proximal anastomosis was necessary, it was performed in 'no touch' fashion using the heartstring device (HEARTSTRING™ Proximal Seal System, Guidant, Indianapolis, USA). After LIMA to LAD grafting, the right coronary system was approached, and finally the circumflex territory was addressed. Standardized ultrasound flow measurement (MediStim QuickFit®) was carried out in all patients [15].

Completeness of revascularization

The anticipated complete revascularization was based on the defined target vessels reported on the preoperative angiography. This information was compared to the performed grafts documented in the postoperative surgical report and was assumed to be complete when the total number of distal grafts was higher than that of diseased vessels reported on the preoperative angiography [7].

Statistical analysis

Endpoints analyzed are mortality and major adverse cardiac and cerebrovascular events (MACCE). A composite endpoint including major non-cardiac adverse events such as respiratory failure, renal failure, and rethoracotomy for bleeding was created. Crossover patients were analyzed on an '*Intention-to-treat*' basis.

Continuous data are presented as mean ± standard deviation and are compared using the Mann–Whitney test. Categorical data are presented as number and percentage and are compared using the Chi-square test or Fisher's exact test where appropriate. Odds ratios with 95% confidence intervals are computed using univariate logistic regression. A propensity score (PS) was calculated using logistic regression with preoperative variables to balance characteristics between both groups. In case of missing values in preoperative variables were replaced using regression methods. The PS then was divided into quintiles and analyzed as a categorical variable. PS-adjusted logistic regression analysis was performed to assess binary endpoints and two-way analysis of variance for continuous endpoints.

The data-set of preoperative variables for the PS score included preoperative patient characteristics such as cardiovascular risk-factors and co-morbidities including cerebral-vascular events, peripheral artery disease (PAD), chronic-obstructive pulmonary-disease (COPD), and renal disease. These parameters were defined in accordance with the definitions of the EuroScore Risk Stratification system (http:\\www.euroscore.org); Cerebrovascular disease defined as the history of transient ischemic attacks (TIA) or stroke, COPD defined with the long-term use of bronchodilators or steroids for lung disease, renal disease as creatinine levels >200 μmol/l and PAD defined as one or more of claudication, carotid occlusion or >50% stenosis, previous or planned intervention on the abdominal aorta, limb arteries or carotids. Diabetes mellitus was defined as type 2 insulin-dependant diabetes (Table 2).

Cardiac-related preoperative conditions were: preceding myocardial-infarction (MI), recent MI within 3 months prior to surgery, preceding cardiogenic-shock, congestive heart-failure, instable angina pectoris, arrhythmias, number of diseased coronary-vessels, previous CABG, elective, urgent/or emergent presentation, previous PTCA, previous stent implantation, NYHA class, CCS class, logistic EuroScore and others. All analyses were performed using SPSS 18 (SPSS Inc., Chicago, IL, USA). p values <0.05 are assumed to be statistically significant.

Results

Patient demographics

OPCAB patients and CABG patients were comparable with regards to mean age, gender, and EuroScore. In brief, OPCAB patients presented with significantly more peripheral artery disease (18.3 vs. 11.3%; $p = 0.039$) and diabetes (35.2 vs. 22.5%; $p = 0.003$), whereas patients undergoing on-pump CABG suffered more frequently from chronic obstructive pulmonary disease (COPD) (4.7 vs. 10.4%; $p = 0.022$) and presented more frequently with instable angina (14.7 vs. 27.5%; $p = 0.005$). The number of patients presenting with significant left main disease (28.5 vs. 23.9%; $p = 0.26$) or for redo surgery (5.5 vs. 4.5%; $p = 0.68$) was comparable in both groups.

Table 2 Risk factors and co-morbidities

Parameter	OPCAB $n = 256$	CABG $n = 222$	p value
Hypercholesterolemia (%)	65.0	71.6	0.20
Hypertension (%)	58.1	50.4	0.10
Positive family history (%)	32.0	32.0	1.00
Diabetes	35.2	22.5	0.003
Smoking (%)	61.0	59.5	0.76
Adiposities (%)	48.8	41.0	0.09
PAD (%)	18.3	11.3	0.039
COPD (%)	4.7	10.4	0.022
Recent myocardial infarction (<90 days) (%)	20.7	31.5	0.009
Previous MI (>90 days) (%)	48.0	59.9	0.01
Previous cardiogenic shock (>90 days) (%)	14.7	17.1	0.56
Cerebrovascular disease (%)	2.0	0.0	0.06
Previous syncope (%)	5.6	1.4	0.03
Renal disease (%)	4.2	4.5	1.00
Instable angina (%)	14.7	27.5	0.005
IABP preoperative (%)	18.8	25.2	0.09

PAD peripheral artery disease, *COPD* chronic obstructive pulmonary disease, *MI* myocardial infarction, *IABP* intra aortic balloon pump

Outcome data before and after propensity adjustment (Table 3)

OPCAB patients had a comparable mortality rate (2.3 vs. 4.1%; odds ratio (OR) = 0.57; 95% CI 0.20–1.62; p = 0.29) and similar MACCE (13.7 vs. 17.6%; OR = 0.74; 95% CI 0.44–1.22; p = 0.24) such as myocardial infarction (1.4 vs. 4.1%; OR = 0.34; 95% CI 0.71–1.58; p = 0.17) and low cardiac output (2.3 vs. 4.7%; OR = 0.48; 95% CI 0.11–2.23; p = 0.35). The composite of non-cardiac adverse events was lower in the OPCAB group (12.1 vs. 22.1%; OR = 0.49; 95% CI 0.30–0.80; p = 0.004). This was mainly driven by the reduced occurrence of bleeding complications (6.3 vs. 9.0%; OR = 0.67; 95% CI 0.34–1.33; p = 0.26), renal dysfunction (4.3% vs. 8.1%; OR = 0.50; 95% CI 0.23–1.10; p = 0.08 and respiratory failure (1.1 vs. 4.2%; OR = 0.27; 95% CI 0.33–2.12; p = 0.21). The beneficial effect of OPCAB in regard to respiratory complications was also reflected in a lower rate of pleural effusions and pneumothorax (3.5 vs. 7.5%; OR = 0.25; 95% CI 0.16–1.25; p = 0.13) as well as in the overall shorter time to extubation (<12 h) (58.9 vs. 36.9%; OR = 2.44; 95% CI 1.63–3.65; $p < 0.001$) indicating a more straight-forward postoperative course. Neurological outcomes including the occurrence of stroke were comparable in both groups (2.3 vs. 2.7%; OR = 0.86; 95% CI 0.28–2.72; p = 0.80).

After propensity score adjustment, OPCAB patients still displayed comparable mortality (propensity-adjusted odds ratio (PAOR) = 1.05; 95% CI 0.30–3.63; p = 0.93) and MACCE (PAOR = 1.22; 95% CI 0.68–2.22; p = 0.50). In regard to the non-cardiac complications including renal dysfunction (PAOR = 0.77; 95% CI 0.31–1.9; p = 0.57), bleeding (PAOR = 0.42; 95% CI 0.14–1.20; p = 0.10) and respiratory failure (PAOR = 0.39; 95% CI 0.05–3.29; p = 0.39), the beneficial effect of OPCAB remained visible. Similarly, a trend towards less occurrence of the non-cardiac composite was still detectable for OPCAB, however, failed to achieve statistical significance after adjustment (PAOR = 0.0.54; 95% CI 0.29–1.02; p = 0.059).

Intra-operative data and completeness of revascularization (Table 4)

The need for intra-operative implantation of an IABP was similar in both groups (5.9 vs. 7.2%; p = 0.32). Conversion to CPB became necessary in 5.9% of all OPCAB patients. If converted, the operation was continued in beating-heart fashion.

Table 3 Crude outcome and propensity adjusted outcome

Parameter	OPCAB $n = 256$	CABG $n = 222$	OR	CI 95%	p value	PA OR	PA CI 95%	PA p value
Mortality (%)	2.3	4.1	0.57	0.20–1.62	0.29	1.05	0.30–3.63	0.93
Neurological events (central) (%)	2.3	2.7	0.86	0.28–2.72	0.80	0.69	0.14–3.54	0.66
Neurological events (peripheral) (%)	1.2	0.5	2.62	0.27–25.37	0.40	1.14	0.07–18.84	0.93
Re-thoracotomy for bleeding (%)	6.3	9.0	0.67	0.34–1.33	0.26	0.42	0.14–1.20	0.10
Myocardial infarction (%)	1.4	4.1	0.34	0.71–1.58	0.17	0.39	0.07–2.01	0.26
Low cardiac output (%)	2.3	4.7	0.48	0.11–2.23	0.35	0.75	0.15–3.70	0.72
Graft occlusion (%)	0.0	1.9	–	–	0.32	–	–	0.32
Cardiac tamponade (%)	0.0	0.5	–	–	1.00	–	–	1.00
Arrhythmia (%)	6.9	3.7	1.91	0.64–5.67	0.24	2.15	0.63–7.30	0.22
IABP postop (%)	0.0	2.7	–	–	**0.01**	–	–	0.01
Renal dysfunction (%)	4.3	8.1	0.50	0.23–1.10	0.08	0.77	0.31–1.90	0.57
No ventilation (%)	1.0	0.9	1.12	0.16–7.99	0.91	6.96	0.91–53.11	0.61
Ventilation <12 h (%)	58.9	36.9	2.44	1.63–3.65	**<0.001**	1.39	0.79–2.43	0.25
Prolonged ventilation >24 h (%)	8.3	11.7	0.69	0.36–1.33	0.27	1.59	0.70–3.42	0.27
Respiratory failure (%)	1.1	4.2	0.27	0.33–2.12	0.21	0.39	0.05–3.29	0.39
Pleural effusions/pneumothorax (%)	3.5	7.5	0.25	0.16–1.25	0.13	0.56	0.19–1.66	0.30
Sinus rhythm (%)	87.4	93.7	0.47	0.22–0.97	**0.04**	0.52	0.23–1.18	0.12
Atrial fibrillation (%)	9.1	5.9	1.60	0.72–3.57	0.24	1.90	0.80–4.48	0.15
MACCE (%)	13.7	17.6	0.74	0.45–1.22	0.24	1.22	0.68–2.20	0.50
Non-cardiac composite (%)	12.1	22.1	0.49	0.30–0.80	**0.004**	0.54	0.29–1.02	**0.059**

OR odds ratio, *95% CI* confidence interval 95%, *PA OR* propensity adjusted OR, *PA 95% CI* propensity adjusted 95% CI, *PA p value* propensity adjusted p value, *IABP* Intra-aortic balloon pump, *MACCE* major adverse cardiac and cerebrovascular events

Table 4 Intraoperative data

Parameter	OPCAB $n = 256$	CABG $n = 222$	p value
CPB conversion (%)	5.9	–	–
CPB time (min)	–	107 ± 46	–
Aortic x-clamp time (min)	–	48 ± 27	–
Arterial grafts per patient	1.49 ± 0.98	1.35 ± 0.80	**0.28**
LIMA (%)	96.9	95.0	0.67
RIMA (%)	30.9	26.6	**0.73**
Radial artery (%)	16.0	3.6	**<0.001**
SVG per patient	1.93 ± 1.28	2.50 ± 1.10	**<0.001**
Use of SVG (%)	81.6	89.2	**0.037**
Total number of proximal anastomoses	1.12 ± 0.61	1.44 ± 0.64	**0.05**
Total number of grafts per patient	3.42 ± 1.05	3.85 ± 0.81	**<0.001**
No of diseased vessels	2.79 ± 0.45	2.95 ± 0.23	**0.001**
Completeness of revascularization (%)	92.2	92.8	0.50
IABP intraoperative (%)	5.9	7.2	0.32

OPCAB patients presented with a lower mean number of the diseased coronary vessels (2.79 ± 0.45 vs. 2.95 ± 0.23; $p = 0.001$) and also received a lower number of total distal grafts (3.42 ± 1.05 vs. 3.85 ± 0.81; $p < 0.001$). For similar proportions in both groups, revascularization was possible without necessity of any proximal anastomosis (9.8 vs. 10.8%; $p = 0.42$). Complete revascularization was achieved in similar levels for both groups (92.2 vs. 92.8%; $p = 0.50$).

Discussion

OPCAB is safe and feasible in high-risk patients with severely decreased EF requiring myocardial revascularization. Mortality and MACCE are comparable to patients undergoing on-pump surgery. Furthermore, our results highlight that OPCAB patients presented with a trend to less non-cardiac complications, including renal dysfunction and postoperative bleeding. These patients also appeared to have decreased respiratory complications, which was also reflected in an overall faster extubation indicating a straighter postoperative course.

Although a recent prospective randomized trial identified OPCAB to have no advantage in low-risk patients [16], it appears to be the superior method of revascularization in high-risk patients [9, 17, 18].

Our results are in line with Stamou et al. [17] who recently reviewed 513 high-risk patients. Of these patients, 228 presented with an EF <34% either undergoing on-pump CABG ($n = 102$) or off-pump CABG ($n = 126$). They identified OPCAB to have a lower mortality and a comparable event-free survival. The authors concluded that off-pump CABG can be performed with a reasonably low morbidity and lower mortality in high-risk patients. In comparison to our study, Stamou et al. [17] did not specifically focus on the outcome of patients with low EF, but on patients with a generally high-risk profile, including factors such as renal-failure, recent myocardial-infarction, cerebrovascular disease and advanced age.

Among 1,398 evaluated high-risk patients, Al-Ruzzeh et al. [18] identified OPCAB patients to have significantly less major postoperative complications. Puskas and colleagues [9] compared 14,766 patients and found that OPCAB is associated with a lower operative mortality and disproportionately benefits high-risk patients.

Very similar to our report, Sharoni et al. recently evaluated 353 patients with an EF <35% who either underwent OPCAB ($n = 144$) or on-pump ($n = 209$) coronary artery bypass surgery. Both groups did not differ significantly in regard to major postoperative complication rates or mortality suggesting OPCAB to be applicable for patients with impaired left ventricular function. The authors showed an increase in the use of OPCAB over time, without any impact on morbidity or mortality [19]. This is in line with our results and is well comparable to the evolution of OPCAB as the standard of care at many institutions.

Cardiopulmonary bypass may have a damaging effect on the myocardium. Pathophysiologically, this is reflected by an extended degree of inflammatory response [4] and myocardial injury [20, 21], especially if the CPB run is prolonged [10]. The activation of numerous inflammatory mediators may compromise myocardial performance, particularly if the LV function is already severely impaired [22, 23]. Moreover, due to the transient change of the ventricular geometry and the ischemic cardiac arrest during CPB, the coronary collateral-flow supplying ischemic areas of the myocardium, is limited [23]. Therefore, OPCAB may be beneficial for patients with severely decreased EF with regards to an overall better cardiac recovery and straighter postoperative course.

A standardized OPCAB approach in high-risk patients does not come at a price of less complete revascularization. This is an important aspect that has been highlighted to be a crucial predictor for the long-term outcome [7, 8], but has also been reported to be a major argument against OPCAB [11, 24, 25]. Our findings are supported by Puskas et al. [8] who demonstrated feasibility of complete revascularization using OPCAB.

Due to its retrospective nature and non-randomized design, all established disadvantages apply. Although balancing scores constitute the most rigorous methods available for apples-to-apples investigation of causal effects on outcome in the retrospective, nonrandomized setting, they are not equal to randomized clinical trials and they cannot account for unknown variables affecting outcome that are not correlated strongly with measured variables [26]. In addition, our results lack the force of numbers and certainly a higher level of significance may have been achieved, had we had a larger patient cohort to analyze. Although the total number of diseased vessels was included in the propensity adjustment, a certain bias may apply, since OPCAB patients had significantly less diseased vessels. Finally, the study period was quite long with most CABG patients being from the early part of the study, whereas the major part of OPCAB patients was from the later part of the study period.

In conclusion, OPCAB in high-risk patients with severely decreased EF is safe and should not deter surgeons from performing the OPCAB approach in this subset of patients. It comes with similar mortality and MACCE, may even benefit the patients in regard to non-cardiac complications and is not at cost of less complete revascularization.

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